

AMENDMENTS TO THE CLAIMS

The following listing of claims replaces all prior versions, and listings, of claims in this application.

Claim 1 (withdrawn): A method for treating a patient with cancer in which TCF/ β catenin signaling is deregulated comprising administering a therapeutic composition to said patient comprising an inhibitor of the expressed protein, or peptide derived therefrom, of a TCF target gene whose expression is regulated by a TCF/ β catenin complex.

Claim 2 (withdrawn): The method of claim 1, wherein the inhibitor is an antibody or derivative thereof directed against the expression product of the target gene that is expressed on the cell membrane.

Claim 3 (withdrawn): The method of claim 1, wherein the antibody or derivative thereof is directed against a peptide, which is chosen from the group consisting of: H-YEKELSEYNATALKSPC-NH₂; H-PFSPQFASVNC-NH₂; H-PGSYKAKQGEGPC-NH₂; H-CQMNSVQLDGLPDARY-OH; H-CGYDARQKPEVDQQ-OH; H-CKGVLSNISSITDLGGFD-OH; H-HSALEDVEALHPRKERC-NH₂; and H-CNYHSHAGAREHRRGD-OH.

Claim 4 (withdrawn): The method of claim 3, wherein the derivative is selected from the group consisting of scFv fragments, Fab fragments, chimeric antibodies, bifunctional antibodies, and other antibody-derived molecules.

Claim 5 (withdrawn): The method of claim 1, wherein the inhibitor is a small molecule that interferes with the biological activity of the protein expressed by the target gene.

Claim 6 (withdrawn): A method for treating a patient with cancer in which TCF/ β catenin signalling is deregulated comprising administering a therapeutic composition to said patient comprising an inhibitor of the mRNA transcript of a TCF target gene whose expression is regulated by a TCF/ β catenin complex.

Claim 7 (withdrawn): The method of claim 6, wherein the inhibitor is an antisense molecule, in particular antisense RNA or antisense oligodeoxynucleotides.

Claim 8 (withdrawn): The method of claim 6, wherein the inhibitor is a double stranded RNA molecules for RNA interference.

Claim 9 (withdrawn): The method of claim 6, wherein the treatment comprises gene therapy.

Claim 10 (withdrawn): The method of claim 1 or 6, wherein the therapeutic composition is for treatment of Familial Adenomatous Polyposis (FAP).

Claim 11 (withdrawn): The method of claim 1 or 6, wherein the therapeutic composition is for treatment of colorectal cancer.

Claim 12 (withdrawn): The method of claim 1 or 6, wherein the therapeutic composition is for treatment of melanomas.

Claim 13 (canceled)

Claim 14 (withdrawn): A method for diagnosing a patient with cancer in which TCF/ β catenin signaling is deregulated wherein the diagnosis is by histological analysis of a tissue specimen using (i) a specific antibody directed against a target gene product, and/or (i) *in situ* hybridization analysis of a TCF/ β -catenin target gene expression levels in tissue specimens using specific RNA probes directed against the TCF/ β -catenin target gene sequence.

Claim 15 (withdrawn): The method of claim 1, 6 or 14, wherein the target gene is selected from the group consisting of CD44, KIT, G protein-coupled receptor 49 (GPR49), Solute Carrier Family 12 member 2 (SLC12A2), Solute Carrier Family 7 member 5, Claudin 1 (CLDN1), SSTK serine threonine kinase, FYN oncogene, EPHB2 receptor tyrosine kinase, EPHB3 receptor tyrosine kinase, EPHB4 receptor tyrosine kinase, ETS2, c-Myc, MYB, ID3, POLE3, Bone Morphogenetic Protein 4 (BMP4), Kit ligand (KITLG), GPX2, GNG2, CDCA7, ENC1, the gene identified with Celera ID hCG40185, the gene identified with Celera ID hCG1645335, the gene represented by IMAGE clone 1871074, the gene identified with Celera ID hCG27486, the gene represented by IMAGE clone 294873, the gene represented by IMAGE clone 940994, the gene identified with Celera ID 39573, the gene represented by IMAGE clone 753028, the gene identified with Celera ID hCG37727, the gene identified with Celera ID hCG40978, and the gene identified with Celera ID hCG1811066.

Claim 16 (withdrawn): The method of claim 1, 6 or 14, wherein the target gene is CD44, comprising a cDNA sequence, which is at least 90% homologous to the cDNA sequence shown in Figure 17 (SEQ. ID. No 1), Figure 18 or Figure 19.

Claim 17 (withdrawn): The method of claim 1, 6 or 14, wherein the target gene is GPR49, comprising a CDNA sequence which is at least 90% homologous to the sequence shown in Figure 20 (SEQ. ID. No 3).

Claim 18 (withdrawn): The method of claim 1, 6 or 14, wherein the target gene is EPBH4, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 21 (SEQ. ID. No 5).

Claim 19 (withdrawn): The method of claim 1, 6 or 14, wherein the target gene is GPX2, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 22 (SEQ. ID. No 7).

Claim 20 (withdrawn): The method of claim 1, 6 or 14, wherein the target gene is RGMR, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 23 (SEQ. ID. No 9).

Claim 21 (withdrawn): The method of claim 1, 6 or 14, wherein the target gene is Tspan5, represented by a sequence which is at least 90% homologous to the sequence shown in Figure 24 (SEQ. ID. No 11).

Claim 22 (withdrawn): The method of claim 1, 6 or 14, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences as shown in Figure 17 or 18.

Claim 23 (withdrawn): The method of claim 1, 6 or 14, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 20 (SEQ ID No. 4).

Claim 24 (withdrawn): The method of claim 1, 6 or 14, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 21 (SEQ ID No. 6).

Claim 25 (withdrawn): The method of claim 1, 6 or 14, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 22 (SEQ ID No. 8).

Claim 26 (withdrawn): The method of claim 1, 6 or 14, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 23 (SEQ ID No. 10).

Claim 27 (withdrawn): The method of claim 1, 6 or 14, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 24 (SEQ ID No. 12).

Claim 28 (withdrawn): Inhibitor compound directed against the expressed proteins, or peptides derived therefrom, of a TCF target gene the expression of which is regulated by a TCF/ β -catenin complex.

Claim 29 (withdrawn): The inhibitor-compound of claim 28, wherein said inhibitor compound is an antibody or derivative thereof directed against the expression products of a target gene that is expressed on a cell membrane.

Claim 30 (withdrawn): The inhibitor compound of claim 29 wherein the antibodies or derivatives thereof are directed against a peptide, which is chosen from the group consisting of: H-YEKELSEYNATALKSPC-NH₂; H-PFSPQFASVNC-NH₂; H-PGSYKAKQGEGPC-NH₂; H-CQMNSVQLDGLPDARY-OH; H-CGYDARQKPEVDQQ-OH; H-CKGVLNMISSITDLGGFD-OH; H-HSALEDVEALHPRKER-C-NH₂; and H-NYHSHAGAREHRRGD-OH.

Claim 31 (withdrawn): The inhibitor compound of claim 29, wherein the derivative is selected from the group consisting of scFv fragments, Fab fragments, chimeric antibodies, bifunctional antibodies, or other antibody-derived molecules.

Claim 32 (withdrawn): The inhibitor compound of claim 28, wherein said inhibitor compound is a small molecule that interferes with the biological activity of the protein expressed by the target gene.

Claim 33 (withdrawn): The inhibitor compound directed against the transcription product (mRNA) of a TCF target gene the expression of which is regulated by TCF/ β -catenin complexes.

Claim 34 (withdrawn): The inhibitor compound of claim 33, wherein said inhibitor compound is an antisense molecule, that is an antisense RNA or an antisense oligodeoxynucleotide.

Claim 35 (withdrawn): The inhibitor compound of claim 34, wherein said inhibitor compound is a double stranded RNA molecule for RNA interference.

Claim 36 (withdrawn): The inhibitor compound of claims 28 or 33, wherein the target gene is selected from the group consisting of CD44, KIT, G protein-coupled receptor 49 (GPR49), Solute Carrier Family 12 member 2 (SLC12A2), Solute Carrier Family 7 member 5, Claudin 1 (CLDN1), SSTK serine threonine kinase, FYN oncogene, EPHB2 receptor tyrosine kinase, EPHB3 receptor tyrosine kinase, EPHB4 receptor tyrosine kinase, ETS2, c-Myc, MYB, ID3, POLE3, Bone Morphogenetic Protein 4 (BMP4), Kit ligand (KITLG), GPX2, GNG2, CDCA7, ENC1, the gene identified with Celera ID hCG40185, the gene identified with Celera ID hCG1645335, the gene represented by IMAGE clone 1871074, the gene identified with Celera ID hCG27486, the gene represented by IMAGE clone 294873, the gene represented by IMAGE clone 940994, the gene identified with Celera ID 39573, the gene represented by IMAGE clone 753028, the gene identified with Celera ID hCG37727, the gene identified with Celera ID hCG40978, and the gene identified with Celera ID hCG1811066.

Claim 37 (withdrawn): The inhibitor compound of claim 28 or 33, wherein the target gene is CD44, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 17 (SEQ. ID. No 1), Figure 18, or Figure 19.

Claim 38 (withdrawn): The inhibitor compound of claim 28 or 33, wherein the target gene is GPR49, comprising a CDNA sequence which is at least 90% homologous to the sequence shown in Figure 20 (SEQ. ID. No 3).

Claim 39 (withdrawn): The inhibitor compound of claim 28 or 33, wherein the target gene is EPBH4, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 21 (SEQ. ID. No 5).

Claim 40 (withdrawn): The inhibitor compound of claim 28 or 33, wherein the target gene is GPX2, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 22 (SEQ. ID. No 7).

Claim 41 (withdrawn – currently amended): The inhibitor compound as claimed in of claim 28 or 33, wherein the target gene is RGMR, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 23 (SEQ. ID. No 9).

Claim 42 (withdrawn): The inhibitor compound Inhibitor compound of claim 28 or 33, wherein the target gene is Tspan5, represented by a sequence which is at least 90% homologous to the sequence shown in Figure 24 (SEQ. ID. No 11).

Claim 43 (withdrawn): The inhibitor compound of claim 28 or 33, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 17 or 18.

Claim 44 (withdrawn): The inhibitor compound of claim 28 or 33, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 20 (SEQ ID No. 4).

Claim 45 (withdrawn): The inhibitor compound of claim 28 or 33, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 21 (SEQ ID No. 6).

Claim 46 (withdrawn): The inhibitor compound of claim 28 or 33, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 22 (SEQ ID No. 8).

Claim 47 (withdrawn): The inhibitor compound of claim 28 or 33, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 23 (SEQ ID No. 10).

Claim 48 (withdrawn): The inhibitor compound of claim 28 or 33, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 24 (SEQ ID No. 12).

Claim 49 (withdrawn): Diagnostic agent for diagnosing cancers in which TCF/ β -catenin signaling is deregulated.

Claim 50 (withdrawn): The diagnostic agent of claim 49, which is a specific antibody directed against the expressed protein of a TCF/ β -catenin target gene or an RNA probe specific for a TCF/ β -catenin target gene sequence.

Claim 51 (withdrawn): Therapeutical composition for the treatment of cancer in which the TCF/ β -catenin signaling is deregulated, comprising a suitable excipient, carrier and/or diluent and one or more of the inhibitor compounds of claims 28 and 33.

Claim 52 (withdrawn): Diagnostic composition for the diagnosis of cancer in which the TCF/ β -catenin signaling is deregulated, comprising a suitable excipient, carrier and/or diluent and one or more diagnostic compounds as claimed in claim 49 or 50.

Claim 53 (withdrawn): The compositions of claim 51 or 52, wherein the cancer is colorectal cancer, melanoma or Familial Adenomatous Polyposis (FAP).

Claim 54 (currently amended): ~~Method~~ A method for the development of a therapeutic inhibitor compound[[s]] ~~as claimed in~~ as set forth in claim 28 or 33, ~~which the method comprises~~ comprising the steps:

- a) ~~identification of~~ identifying one or more genes regulated by TCF/ β -catenin in colon carcinoma cells, ~~in particular~~ by using microarray technologies;
- b) ~~validation of~~ validating one or more of the identified genes as one or more potential target gene(s) genes for the therapeutic compound by one or more of the following methods selected from the group consisting of:
 - ~~[[-]] (i) confirmation of~~ confirming the identified gene by Northern Blot analysis in colon carcinoma cell-lines;
 - ~~[[-]] (ii) determination of~~ determining the expression profile of the identified gene in human colorectal tumors and normal tissue; and
 - ~~[[-]] (iii) determination of~~ determining the functional importance of the identified target gene[[s]] for colorectal cancer;
- c) ~~production of~~ producing the expression product of the target gene; and
- d) ~~use of~~ using the expression product of the target gene for the production or design of [[a]] the therapeutic compound.

Claim 55 (previously presented): The method of claim 54, wherein the target gene identified in step a) is selected from the group consisting of CD44, KIT, G protein-coupled receptor 49 (GPR49), Solute Carrier Family 12 member 2 (SLC12A2),

Solute Carrier Family 7 member 5, Claudin 1(CLDN1), SSTK serine threonine kinase, FYN oncogene, EPHB2 receptor tyrosine kinase, EPHB3 receptor tyrosine kinase, EPHB4 receptor tyrosine kinase, ETS2, c-Myc, MYB, ID3, POLE3, Bone Morphogenetic Protein 4 (BMP4), Kit ligand (KITLG), GPX2, GNG2, CDCA7, ENC1, the gene identified with Celera ID hCG40185, the gene identified with Celera ID hCG1645335, the gene represented by IMAGE clone 1871074, the gene identified with Celera ID hCG27486, the gene represented by IMAGE clone 294873, the gene represented by IMAGE clone 940994, the gene identified with Celera ID 39573, the gene represented by IMAGE clone 753028, the gene identified with Celera ID hCG37727, the gene identified with Celera ID hCG40978, and the gene identified with Celera ID hCG1811066.